ACUTE FUNCTIONAL TOLERANCE TO ETHANOL IN MICE SELECTIVELY BRED FOR HIGH AND LOW ALCOHOL PREFERENCE DRINKING

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Propensity to develop acute functional (or within session) tolerance to alcohol (ethanol) may influence the amount of alcohol consumed, with higher drinking associated with greater acute functional tolerance (AFT). The goal of the current study was to assess this potential correlated response in second and third replicate lines of mice selectively bred for high (HAP2&3) and low (LAP2&3) alcohol preference drinking. We predicted that HAP mice would develop greater AFT to alcohol's ataxic actions than LAP mice. Male and female HAP2&3 and LAP2&3 mice were tested for development of AFT on a static dowel task. This task requires that animals maintain balance on a wooden dowel in order to prevent falling. On test day, each mouse received one (1.75g/kg; experiment 1) or two (1.75g/kg and 2.0g/kg; experiment 2) injections of ethanol; an initial administration before being placed on the dowel and in another experiment, an additional administration after the first regain of balance on the dowel. Blood samples were taken immediately after loss of balance and regain in Experiment, 1 and after first and second regain in Experiment 2. It was found that HAP mice fell from the dowel significantly earlier and at lower BACs than LAP mice following the initial injection of ethanol and were therefore more sensitive. Furthermore, the single-injection experiment detected significantly greater AFT development (BAC2-BAC1) in HAP mice as compared to LAP mice, supporting our hypothesis. This study illustrates the rapidity with which adaptive pharmacodynamic processes can take place which may contribute to excessive alcohol consumption.

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